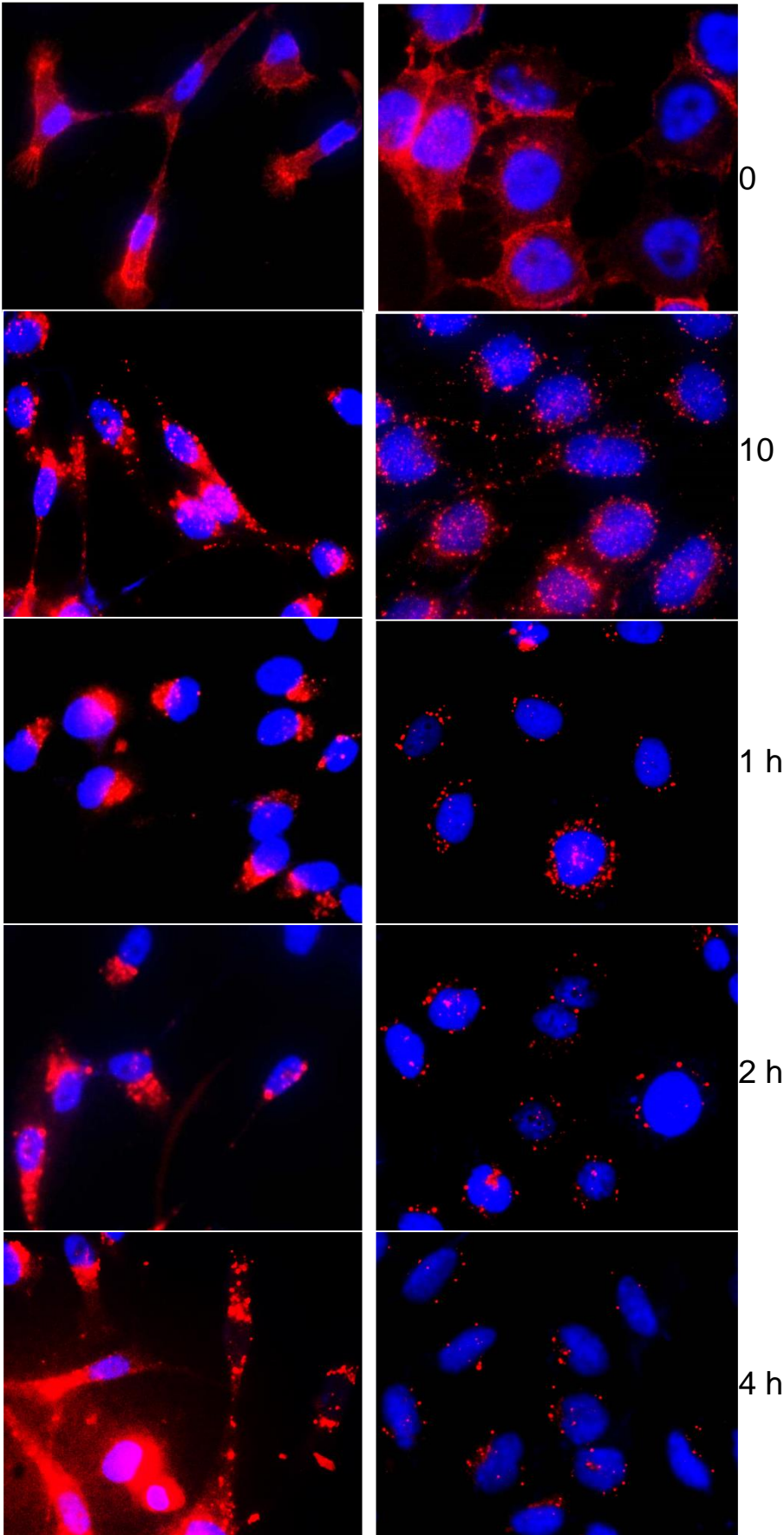
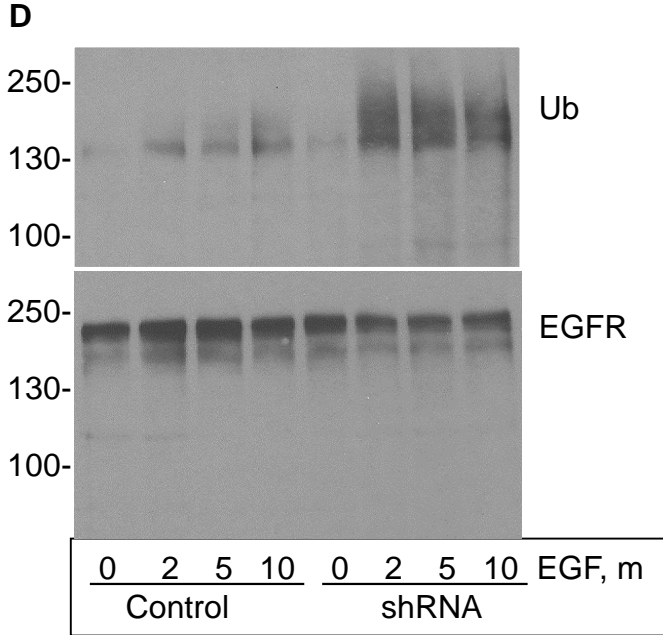


**Supplementary figure 3a and b:** Dynamics of EGFR degradation in the MDA-MB231 cells in the presence and absence of SHP2. **a)** First, EGFR was stabilized by chloroquine treatment for 6 hours and then cells were stimulated with 10 ng/ml EGF for the indicated time points. Lysates prepared from these cells were analyzed by immunoblotting with anti-EGFR antibody. As shown, EGFR was degraded relatively rapidly in the SHP2-silenced cells, but not in the control. The anti-SHP2 and the anti-β-actin immunoblotting show efficient SHP2 silencing and comparable total protein loading, respectively. **b)** Band density measurement of the EGFR immunoblotting. As shown, approximately 75% of EGFR in the SHP2-silenced cells was degraded within 1 hour, but only 30% was degraded in the controls even at the 4 hour time point. Data shown is mean ± standard error from three independent experiments.

**c**

**Supplementary figure 3c:** Effect of SHP2 silencing on EGFR endocytosis and processing in the MDA-MB231 cells. EGF-induced EGFR endocytosis was not affected by SHP2 silencing, but the processing thereafter. While EGFR in the controls was sorted in polarized fashion with gradual outward extension, it remained perinuclear in the SHP2 silenced cells. In addition, it was possible to discern the rapid dissipation of the EGFR signal in the SHP2 silenced cells, but not in the controls.



**Supplementary figure 3D:** Effect of SHP2 silencing on EGFR ubiquitination in the MDA-MB231 cells. First, EGFR was stabilized by chloroquine treatment for 6 hours and then cells were stimulated with 10 ng/ml EGF for the indicated time points. Lysates prepared from these cells were subjected to immunoprecipitation with anti-EGFR and immunoblotting with anti-ubiquitin antibodies. To compensate for the partial nature of EGFR restoration by chloroquine, the amount of EGFR precipitate loaded in the shRNA lanes was increased by 25%. As shown, EGFR was rapidly and highly ubiquitinated in the SHP2 silenced cells, but less so in the controls. Reprobing with anti-EGFR antibody showed comparable protein levels in all lanes.